

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 February 1999 (03.02.99)

International application No. PCT/US98/08646	Applicant's or agent's file reference PCT 19962Y
International filing date (day/month/year) 04 June 1998 (04.06.98)	Priority date (day/month/year) 05 June 1997 (05.06.97)

Applicant ROSEN, Neal et al

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

11 December 1998 (11.12.98)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Christelle Croci
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A01N 43/50, 43/60, A61K 31/415, 31/495		A1	(11) International Publication Number: WO 98/54966 (43) International Publication Date: 10 December 1998 (10.12.98)
 (21) International Application Number: PCT/US98/08646 (22) International Filing Date: 4 June 1998 (04.06.98) (30) Priority Data: 60/048,736 5 June 1997 (05.06.97) US 9801231.3 21 January 1998 (21.01.98) GB			GAST, George, C. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). (74) Common Representative: MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). (81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).
 (71) Applicants (for all designated States except US): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH [US/US]; 1275 York Avenue, New York, NY 10021 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): ROSEN, Neal [US/US]; 1275 York Avenue, New York, NY 10021 (US). SEPP-LORENZINO, Laura [AR/US]; 1275 York Avenue, New York, NY 10021 (US). MOASSER, Mark, M. [US/US]; 1275 York Avenue, New York, NY 10021 (US). OLIFF, Allen, I. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). GIBBS, Jackson, B. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). KOHL, Nancy [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). GRAHAM, Samuel, L. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). PRENDER-			 Published <i>With international search report.</i>
 (54) Title: A METHOD OF TREATING CANCER (57) Abstract The present invention relates to methods of treating cancer using a combination of a compound which is an antineoplastic agent and a compound which is an inhibitor of prenyl-protein transferase, which methods comprise administering to said mammal, either sequentially in any order or simultaneously, amounts of at least two therapeutic agents selected from a group consisting of a compound which is an antineoplastic agent and a compound which is an inhibitor of prenyl-protein transferase. The invention also relates to methods of preparing such compositions.			

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EE	Estonia						

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US98/08646

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A01N 43/50, 43/60; A61K 31/415, 31/495

US CL : 514/255, 396, 397, 400

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/255, 396, 397, 400

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Database WPIDS, London: Derwent Publications Ltd., AN 91-334169/46, EP 456180 A (SQUIBB & SONS INC.) "Assaying farnesyl-protein transferase - by measuring incorporation of farnesyl residues into ras protein substrate, identifying cpds. which block neoplastic transformation." 13 November 1991, see entire abstract.	1-32

Further documents are listed in the continuation of Box C. See patent family annex.

- * Special categories of cited documents:
- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "A" document defining the general state of the art which is not considered to be of particular relevance
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "E" earlier document published on or after the international filing date
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed
- "&" document member of the same patent family

Date of the actual completion of the international search

26 JULY 1998

Date of mailing of the international search report

08SEP1998

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

REC'D 13 APR 1999

WIPO PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PCT 19962Y	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US98/08646	International filing date (<i>day/month/year</i>) 04 JUNE 1998	Priority date (<i>day/month/year</i>) 05 JUNE 1997
International Patent Classification (IPC) or national classification and IPC IPC(6): A01N 43/50, 43/60; A61K 31/415, 31/495 and US Cl.: 514/255, 396, 397, 400		
Applicant MERCK & CO., INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets.

This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 11 DECEMBER 1998	Date of completion of this report 11 MARCH 1999
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile N . (703) 305-3230	Authorized Officer FREDERICK KRASS Telephone N . (703) 308-1235 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/08646

I. Basis of the report

1. This report has been drawn on the basis of (*Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments*):

- the international application as originally filed.
- the description, pages 1-300, as originally filed;
pages NONE, filed with the demand.
pages NONE, filed with the letter of _____.
pages , filed with the letter of _____.
- the claims, Nos. 1-32, as originally filed.
Nos. NONE, as amended under Article 19.
Nos. NONE, filed with the demand.
Nos. NONE, filed with the letter of _____.
Nos. , filed with the letter of _____.
- the drawings, sheets/fig 1-33, as originally filed.
sheets/fig NONE, filed with the demand.
sheets/fig NONE, filed with the letter of _____.
sheets/fig , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

- the description, pages NONE.
- the claims, Nos. NONE.
- the drawings, sheets/fig NONE.

3. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/08646

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)	Claims <u>1-32</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-32</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-32</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-32 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest compositions comprising a combination of a prenyl-transferase inhibitor and an antineoplastic agent, nor therapies in which a prenyl-transferase inhibitor is combined with conventional adjunct cancer therapies. Furthermore, the prior art does not recognize the unexpected advantages of such combined therapies, for example synergistic effect and lower toxicity as discussed at pages 16 and 17 of the description.

Claims 1-32 meet the criteria set out in PCT Article 33(4); the industrial applicability of the claimed compositions and methods to the pharmaceutical/medical industries is self-evident.

----- NEW CITATIONS -----
NONE